REMARKS

Reconsideration of the present application is respectfully requested in view of the Amendment submitted herewith and the following remarks. Claims 3-10 and 13-19 were pending in the Application. Claims 3-6, 9, and 16 have been amended to point out with more particularity and to claim distinctly certain embodiments of Applicants' invention. Claim 7 is hereby cancelled. Claims 3-6, 8-10, and 13-19 are therefore currently under examination. The above Amendment is not to be construed as acquiescence to the stated grounds for rejection and is made without prejudice to prosecution of any subject matter modified or removed by this Amendment in a related divisional, continuation, or continuation-in-part application. No new matter has been added to the application. Support for the amended claims may be found throughout the specification, for example, at page 14, lines 10-14; and page 15, lines 10-15.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT)

In this Office Action the Examiner has rejected claims 3-5, 7-10, and 13-19 under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. The Examiner asserts that the scope of the claims is not commensurate with the subject matter enabled by the disclosure. The Examiner asserts that the specification does not enable a person skilled in the art to make and use a vaccine composition comprising "at least one (i.e. any) group A Streptococcus antigen and a proteosome adjuvant." (See Action dated June 8, 2006, at page 2, paragraph 4).

Applicants respectfully traverse this rejection and submit that as disclosed in the specification and recited in the instant claims, Applicants fully enabled the presently claimed subject matter at the time the application was filed. Solely to expedite prosecution of certain specific embodiments, Applicants have cancelled claim 7 without acquiescence to this rejection and without prejudice to prosecuting the cancelled subject matter in a related divisional, continuation, or continuation-in-part application.

Applicants respectfully disagree with the assertion by the Examiner that claim 3 relates to a composition that comprises "any" group A Streptococcus antigen. A group A Streptococcal antigen that comprises an antigenic peptide from a particular region of a particular polypeptide, that is, in this instance, an antigenic peptide derived from the conserved C-terminal

region of an *S. pyogenes* M protein, defines the group A antigen with more specificity than "any" group A Streptococcal antigen. Nevertheless, without acquiescing to the rejection and to expedite prosecution of the present application and to point out with even more particularity certain claimed embodiments, claim 3 has been amended herewith to recite, in pertinent part, that the group A Streptococcal antigen comprises an antigenic peptide between 15 and 30 amino acids in length from the conserved C-terminal region of an *S. pyogenes* M protein, wherein the antigenic peptide comprises the amino acid sequence ASREAKKQVEKALE (SEQ ID NO:1) (*see, e.g.*, page 14, lines 4-13; page 15, lines 1-15).

The specification describes that the conserved region in the carboxy terminus that comprises the peptide sequence set forth in SEQ ID NO:1 may be useful for inducing an immune response to more than one serotype of *S. pyogenes* without inducing antibodies that may cross-react with human proteins (*see, e.g.*, page 15, lines 1-27; Figure 1). The present specification further provides in working Examples how to use the claimed compositions for inducing an immune response in a host against group A Streptococcus. The data presented demonstrate the effectiveness of the claimed compositions to reduce group A Streptococcus bacterial load and to protect animals from lethal challenge with group A Streptococcus (*see, e.g.*, Example 4, page 31, line 12 through page 36).

Thus, as provided in the teachings of the application, the specification enables a person skilled in the art to make and use, readily and without undue experimentation, vaccine compositions comprising a proteosome adjuvant and a group A Streptococcal antigen that comprises an antigenic peptide between 15 and 30 amino acids in length from the conserved C-terminal region of an *S. pyogenes* M protein, wherein the antigenic peptide comprises the peptide sequence ASREAKKQVEKALE (SEQ ID NO:1), and wherein the antigen is attached to a hydrophobic moiety (*see, e.g.*, page 15, lines 1-27).

Accordingly, given the disclosure of the present application, which includes several working examples, the specification enables a skilled artisan to make and use the claimed vaccine compositions and methods, readily and without undue experimentation. Applicants therefore respectfully submit that the application satisfies all requirements under 35 U.S.C. § 112, first paragraph, and request that this rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 102

The Examiner has rejected claims 3, 8, 9, 14, and 16 under 35 U.S.C. § 102(b) for allegedly being anticipated by Lowell et al. (*Proteosome and Hydrophobic Foot Vaccines Provide Enhanced Immunogenicity of Malaria, Trypanosome, and Streptococcal Peptides Without Added Adjuvants in* TECHNOLOGICAL ADVANCES IN VACCINE DEVELOPMENT, pp. 423-432 (1988)).

Applicants respectfully traverse this rejection and submit that Lowell et al. fail to teach or suggest each feature of the pending claims; therefore, the document does not destroy the novelty of the presently claimed invention. Lowell et al. do not teach or suggest a vaccine composition comprising a proteosome adjuvant and a group A Streptococcal antigen that comprises an antigenic peptide between 15 and 30 amino acids in length from the conserved C-terminal region of an *S. pyogenes* M protein, wherein the antigenic peptide comprises the peptide sequence ASREAKKQVEKALE (SEQ ID NO:1), and wherein the antigen is attached to a hydrophobic moiety. Lowell et al. instead describe a composition comprising peptides from the amino terminal portions of *S. pyogenes* M6 and M24 proteins that are specific to those respective serotypes (*see* Lowell et al., page 425 and references cited therein).

Accordingly, the cited document fails to anticipate the features of the present claims. Applicants respectfully submit that claims 3, 8, 9, 14, and 16 meet the requirements for novelty under 35 U.S.C. § 102 and request that the rejection of these claims be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 103

The Examiner has rejected claims 4-6 under 35 U.S.C. § 103(a) for allegedly being obvious over Lowell et al. as applied to "claims 1-3, 8, 9, 11, 14, and 16" as set forth in the rejection for lack of novelty, and in further view of Brandt et al. (*Nat. Med.* 6:455-59 (2000)) (*see* Action, page 11, first paragraph). The Examiner has also rejected claims 10 and 13-19 under 35 U.S.C. § 103(a) for allegedly being obvious over Lowell et al. and Brandt et al. as applied to "claims 1-6, 8, 9, 11, 14, and 16," and in further view of Relf et al. (*Adv. Exp. Med. Biol.* 418:859-61 (1997)) (*see* Action, page 13, first paragraph of section 7). Applicants note that claims 1, 2, and 11 were cancelled without prejudice in the Reply and Amendment submitted

March 9, 2006 in response to the Office Action dated November 9, 2005. Applicants, therefore, assume that listing of claims 1, 2, and 11 in this Action was an inadvertent typographical error.

The Examiner asserts that Lowell et al. teach that adjuvants other than alum are needed for human use, that Brandt et al. describe a group A Streptococcal antigen having the amino acid sequences set forth in SEQ ID NO:1 and 2, and that combining the teachings of the cited documents to obtain Applicants' claimed vaccine compositions would be obvious to a person having ordinary skill in the art. With respect to claims 10 and 13-19, the Examiner asserts that Relf et al. teach intranasal administration of a group A Streptococcal vaccine and that by combining the teachings of Relf et al. with Lowell et al. and Brandt et al., a person having ordinary skill in the art would obtain the presently claimed embodiments of Applicants' invention.

Applicants respectfully traverse these rejections and submit that the present claims as amended herewith meet the statutory requirements for nonobviousness under 35 U.S.C. § 103. Applicants submit that the PTO has not established a *prima facie* case of obviousness. *See In re Mayne*, 104 F.3d 1339, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (The PTO has the burden of showing a *prima facie* case of obviousness.). The cited documents, each alone or in any combination, fail to teach or suggest or provide motivation to make a vaccine composition comprising a proteosome adjuvant and a group A Streptococcal antigen that comprises an antigenic peptide between 15 and 30 amino acids in length from the conserved C-terminal region of an *S. pyogenes* M protein, wherein the antigenic peptide comprises the peptide sequence ASREAKKQVEKALE (SEQ ID NO:1), and wherein the antigen is attached to a hydrophobic moiety.

Applicants strongly disagree with the Examiner that a person having ordinary skill in the art would have a reasonable expectation of successfully achieving Applicants' claimed vaccine compositions by combining the teachings of Lowell et al. and Brandt et al. with or without further combining the teachings of Relf et al. Each of the cited documents describes different combinations of antigens and adjuvants that may be used as immunogens for inducing an immune response to group A Streptococcus. Moreover, none of the cited documents teaches

or suggests the desirability of altering either the antigen or adjuvant described in each respective document to achieve the presently claimed vaccine compositions.

As discussed above with respect to the novelty rejection, Lowell et al. describe using proteosomes in combination with peptides from the *amino* terminal portions of the *S. pyogenes* M6 and M24 proteins and which portions are specific to the respective M6 and M24 serotypes (*see* Lowell et al., page 425 and references cited therein). Lowell et al. do not describe or suggest using proteosomes in combination with an antigenic peptide between 15 and 30 amino acids in length from the *conserved C-terminal* region of an *S. pyogenes* M protein, and wherein the peptide antigen comprises the amino acid sequence, ASREAKKQVEKALE.

Brandt et al. fail to teach or suggest a vaccine composition comprising a proteosome adjuvant and further fail to teach or suggest that the group A Streptococcal antigens described therein may be attached to a hydrophobic moiety and combined with a proteosome adjuvant. The description in Brandt et al. that J14 may be combined with Freund's complete adjuvant, an adjuvant routinely used in animal studies provides no suggestion, teaching, or motivation that J14 can successfully be combined with any other adjuvant or with proteosomes in particular.

Moreover, Brandt et al. suggest altering the antigen, not the adjuvant, and describe preparation and use of heteropolymers that combine two or more group A Streptococcus antigens (*see* page 46, last paragraph through page 458). Thus, modification of the teachings of Brandt et al. to combine J14 with proteosomes to achieve Applicants' claimed compositions requires reconstruction and redesign of the immunogen described by Brandt et al. and changes the basic principle for which the immunogen described therein was constructed. (See MPEP 2143.01 (VI) ("If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.")).

Relf et al. in combination with Lowell et al. and Brandt et al. not only fail to teach or suggest the subject matter of claims 10 and 13-19, the combination of references teaches away from the presently claimed compositions. Lowell et al. state that "peptide conjugation to routinely used carriers like tetanus toxoid can result in epitope suppression of peptide immunity"

(page 424, lines 2-11). However, Relf et al. describe that a peptide-specific response in immunized animals to the group A Streptococcus p145 antigen, which is related to J14 (see specification, Figure 2), was "*only observed in mice that received TT [tetanus toxoid] conjugated peptide*" (emphasis added), and conjugation to a different protein, *E. coli* labile toxin subunit B (LTB) "did not successfully induce high titre peptide-specific IgG" (page 860, Results and Discussion). Similarly, as noted above regarding the teachings of Brandt et al., reconstruction and redesign of the immunogen described by Relf et al. changes the basic principle for which the immunogen described therein was constructed. Accordingly, the teachings of the cited documents alone or in any combination provide no motivation and fail to teach or suggest that a person having ordinary skill in the art could reasonably expect to achieve with any success the claimed vaccine compositions.

As previously made of record, while the cited documents suggest a need or desire to obtain a group A Streptococcal vaccine, nowhere do the publications teach or suggest Applicants' solution to the problem. Even assuming, *arguendo,* that the cited documents disclosed each feature of the pending claims, absent some teaching or suggestion to combine features of a claimed invention that are present in the cited art, establishing obviousness on the basis that separate features existed in the prior art is insufficient (*see Ruiz and Foundation Anchoring Systems, Inc. v. A.B. Chance Company*, 234 F.3d 654, 665 (Fed. Cir. 2000)). At best, the assertion of nonobviousness in the Office Action relies on the illegitimate test that a person having ordinary skill in the art might find it "obvious to try" to obtain the claimed compositions using the disclosure of the cited documents. *See In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) ("...[W]hether a particular combination might be "obvious to try" is not a legitimate test of patentability.").

Applicants therefore respectfully submit that a *prima facie* case of obviousness has not been established and that the claimed subject matter is nonobvious as required under 35 U.S.C. § 103. Applicants respectfully request that these rejections of the claims be withdrawn.

Applicants submit that pending claims 3-6, 8-10, and 13-19 are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

Mae Joanne Rosok

Mae Joanne Rosok
Registration No. 48,903

701 Fifth Avenue, Suite 5400
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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